IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 6770
ZAUDERER *et al.*	Art Unit: 1639
Appl. No.: 09/987,456	Examiner: Epperson, J.D.
Filed: November 14, 2001	Atty. Docket: 1821.0070004/EJH/T-M
For: ***In Vitro* Methods of Producing and Indentifying Immunoglobulin Molecules in Eukaryotic Cells**	

Request for Reconsideration of Patent Term Adjustment Determination Under 37 C.F.R. § 1.705(b)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Mail Stop Petitions

Sir:

Applicants herein request reconsideration of the patent term adjustment in the above-captioned application as indicated in the Notice of Allowance dated April 6, 2010. Pursuant to 37 C.F.R. §§ 1.705(b)(1) and (b)(2), Applicants provide a concise statement of facts involved as well as payment of fees set forth in 37 C.F.R. § 1.18(e).

Statement of the Facts:

Applicants hereby request that the Patent Term Adjustment (PTA) for the above-captioned application be corrected to allow an addition of 123 days to the current PTA calculation of 1133 days, the total PTA therefore being one thousand two hundred fifty six (1256) days.

The U.S. Patent and Trademark Office (PTO) mailed a Notice of Allowance and Fee(s) Due on April 6, 2010. This Notice contained a determination of Patent Term Adjustment under 35 U.S.C. § 154(b), which indicated that the PTA up to the date of the Notice of Allowance and Fee(s) Due is one thousand one hundred thirty three (1133) days.

According to PAIR, the calculation of 1133 days is based on a PTO prosecution delay of 253 days (37 C.F.R. § 1.703(a)) reduced by an Applicant delay of 274 days (37 C.F.R. § 1.704(b)) and a PTO appeal delay of 1154 days (37 C.F.R. §

of 274 days (37 C.F.R. § 1.704(b)), and a PTO appeal delay of 1154 days (37 C.F.R. § 1.703(e)). Applicants believe that the PTO delay of 1133 days to date should be increased by one hundred twenty three (123) days under 37 C.F.R. § 1.705(b) (*See also*, 35 U.S.C. §154(b)(3)(B)(ii)). Applicants also believe that the Applicant delay should be increased by seventy (70) days. *See* 37 C.F.R. § 1.705(b)(2)(iv)(A).

Reinstatement of PTA Under 37 C.F.R. §1.705(b) and 35 U.S.C. §154(b)

Applicants believe that 60 of the 126 days of reduction in PTA due to Applicant delay should be reinstated under 37 C.F.R. §1.705(b). PAIR indicates that this delay of 126 days is based on the time period between Applicants' non-compliant Response to a Restriction Requirement dated September 10, 2003, which was filed October 10, 2003, and Applicants' compliant Response, which was filed February 13, 2004. This reduction in PTA is apparently made under 37 C.F.R. § 1.704(c)(7).

Applicants originally replied to the Restriction Requirement on October 10, 2003, one month from the date of mailing. As is shown by the documents in the attached Appendix, the PTO was unexpectedly closed due to a power outage on October 10, 2003. Subsequent follow-up with the 1600 Tech Center on October 31, 2003, revealed that the PTO had misplaced the Response filed on October 10, 2003, and a copy of the Response was sent via facsimile to the Tech Center on that day. Further follow-up with the assigned Examiner for this case on December 11, 2003, revealed that a copy of the Response had not been forwarded to the Examiner and that there was no record of the Response. A copy of the Response as filed was sent to the Examiner via facsimile on December 11, 2003. This facsimile copy of the previously filed Response was miscoded in PAIR as a Supplemental Response. A Notice of Non-Compliant Amendment was then mailed February 11, 2004, four months after the Response was originally filed on October 10, 2003. Applicants filed a Supplemental Response on February 13, 2004.

Applicants believe that PTA for this case should only be reduced to account for the time period from December 10, 2003, which is the date three months from the issuance of the Restriction Requirement, to February 13, 2004, which is the date the compliant Response was filed. This represents a reduction in PTA of 66 days, 60

days less than the current reduction in PTA. Applicants respectfully submit that the current reduction in PTA of 126 days for delays in filing a compliant Response to a Restriction Requirement is counter to the purpose of PTA, which encourages timely filing of responses. Furthermore, 37 C.F.R. § 1.704 (b) provides that Applicants are allowed three months to file a response before a reduction in patent term adjustment is applied. Applicants filed their Response to the Restriction Requirement at the one month deadline, well before the three month date after which deductions in PTA begin to toll. Applicants were then diligent in determining the status of the Response filed, contacting the PTO on multiple occasions to determine if it had been properly docketed. To penalize Applicants for filing the Response promptly would lead to an incongruous result, whereby the Applicants would be eligible for greater PTA if they had waited to file a response three months from the mailing of the Restriction Requirement rather than filing at the one-month shortened statutory period.

Applicants also believe that 63 days of the PTO's delay in docketing Applicants' Response should be counted as PTO delay for the purposes of PTA. This accounts for the time period between Applicants' filing the Response of October 10, 2003, and December 11, 2003, the date on which the Examiner was sent a copy of the Response by facsimile. As is described above, Applicants timely filed the Response under unusual conditions that were not Applicants' fault, and were subsequently diligent in making sure that this response was identified and docketed by the PTO. The delays in prosecution from October 10, 2003, to December 11, 2003, are entirely attributable to the PTO.

In total, adjusting Applicants' reduction in PTA by 60 days and adding 63 days of PTO delay provides an overall change in PTA of 123 days. Applicants believe that 123 days should be added to the current PTA calculation of 1133 days to give a PTA of 1256 days, minus 70 days, as discussed herein below, for a total of 1186 days. Applicants submit that both PTA adjustments described above are equally warranted. However, if the Commissioner is not inclined to make both adjustments, Applicants' respectfully request that at least the 63 days of adjustment for PTO delay be added, since the delays arose through no fault of the Applicants.

***PTO Delay Under 37 C.F.R. §1.702(b), 35 U.S.C. §154(b)(1)(B), and* Wyeth v. Dudas**

In addition, Applicants reserve the right to petition for reconsideration of patent term adjustment due to PTO delay under 37 C.F.R. §1.702(b). Applicants believe that 236 days of PTO delay should be added under 37 C.F.R. §1.702(b). PAIR indicates that 0 days were added for PTO delay under 37 C.F.R. §1.702(b) and 35 U.S.C. §154(b)(1)(B) related to patent prosecution taking more than three years. Three years from the application filing date of November 14, 2001, is November 14, 2004. Applicants note that an RCE was filed on July 21, 2005, thus, no further PTO delay under 37 C.F.R. §1.702(b) is accrued after filing of the RCE (*See* 37 C.F.R. §1.702(b)(1)). From November 14, 2004, to July 21, 2005, there was a PTO delay of 250 days. There was an overlap of 14 days in PTO delay under 37 C.F.R. §§ 1.702(a) and (b) from April 7, 2005, to April 21, 2005 (*See* 35 U.S.C. §154(b)(2)(A)). Therefore, Applicants believe that 236 (250 less 14) days of PTA should be added due to PTO delay under 37 C.F.R. §1.702(b) and 35 U.S.C. §154(b)(1)(B) upon actual issuance of a patent in the above-captioned application.

Applicants' Delay Under 37 C.F.R. §1.704(b)

In addition to the adjustment in the number of days of Applicants delay from October 10, 2003, to February 13, 2004, discussed above, Applicants believe that the information recorded in the PAIR system correctly indicates the following Applicant delays under 37 C.F.R. §1.704(b): a 61-day delay for filing an Information Disclosure Statement (IDS) on July 28, 2004, subsequent to the Response to a Restriction Requirement filed May 28, 2004; a 4-day delay for filing a Response on July 25, 2006, to a Non-Final Office Action dated April 21, 2006; and an 83-day delay for filing an IDS on October 16, 2006, subsequent to the July 25, 2006 Response. Applicants note, however, that the PTA calculation under 37 C.F.R. § 1.702(e) does not account for the 70 days between April 27, 2007, when Applicants filed an Appeal Brief that was deemed to be defective, and July 6, 2007, when Applicants filed an Amended Appeal Brief. Therefore, it is believed that 70 days of

PTA reduction should be subtracted from the total of 1256 days to which Applicants should be entitled (1133 days plus the additional 123 days discussed herein above), for a total of 1186 days. The above-captioned application is not subject to a terminal disclaimer.

37 C.F.R. § 1.705(b)(2)(iii).

Applicants do not believe that there were any circumstances during the prosecution of the application to date that constitute a failure to engage in reasonable efforts to conclude processing or examination of the application as set forth in 37 C.F.R. § 1.704(c) beyond the above-mentioned delays under 37 C.F.R. §1.704(b).

The Precise Relief Requested:

In view of the above, Applicants are entitled, to date, to additional patent term adjustment of a total of at least 123 days. In particular, the total PTO delay of 1133 days is incorrect, and Applicants believe the correct patent term adjustment under 37 C.F.R. §1.702(a) to date is 1186 days.

In accordance with 37 C.F.R. § 1.705(b)(1), the fee set forth in 37 C.F.R. § 1.18(e) is provided *herewith* as a credit card payment. It is not believed that additional fees are required beyond those that may otherwise be provided in documents accompanying this paper. However, if additional fees are required, the U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

If it is believed, for any reason, that personal communication will expedite consideration of this Request, please do not hesitate to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Request is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Tracy L. Muller
Attorney for Applicants
Registration No. 55,472

Date: July 6, 2010

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Appendix

* * * COMMUNICATION RESULT REPORT (OCT. 31. 2003 1:35PM) * * *

TTI SKG&F3712540

ILE MODE	OPTION	ADDRESS (GROUP)	RESULT	PAGE
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REASON FOR ERROR
E-1) HANG UP OR LINE FAIL
E-2) BUSY
E-3) NO ANSWER
E-4) NO FACSIMILE CONNECTION

Sterne Kessler Goldstein Fox
ATTORNEYS AT LAW

Fax

☒Urgent ☒ Return reply requested ☐ Original will be sent as confirmation

To: Patent Technology Center 1600

Date: October 31, 2003

Attention: Renee

Re: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

From: Elizabeth J. Haanes, Ph.D. ejh

Pages (including cover sheet): **30**

Your Reference:

Fax No: 703-308-4407

Our Reference: 1821.0070004/EJH/T-M

Sterne Kessler Goldstein Fox
ATTORNEYS AT LAW

FILE COPY

Fax

☒Urgent ☒ Return reply requested ☐ Original will be sent as confirmation

To: Patent Technology Center 1600

Date: October 31, 2003

Attention: Renee

Re: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

From: Elizabeth J. Haanes, Ph.D.

Pages (including cover sheet): **30**

Your Reference:

Fax No: 703-308-4407

Our Reference: 1821.0070004/EJH/T-M

Message

Per your telephone conversation with Tracy Muller of our office, attached is a copy of the Preliminary Amendment and Reply to Restriction Requirement as filed in person at the U. S. Patent & Trademark Office on Friday, October 10, 2003, along with a copy of the page of the daily filing log book from that date indicating that the filing was delivered.

please sign and return this page as acknowledgment of receipt

If any portion of this transmission is not received clearly or in full,
contact us at 202.371.2600 or f 202.371.2540.

		Due Date:	October 10, 2003
Applicants:	Lerer *et al.*	**Art Unit:**	1639
		Examiner:	Epperson, J.D.
Application No.:	09/987,456	**Docket:**	1821.0070004
Filed:	November 14, 2001	**Atty:**	EJH/T-M

For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. SKGF Cover Letter;
2. Preliminary Amendment Under 37 C.F.R. § 1.115 and Reply to Restriction Requirement; and
3. One (1) return postcard.

Please Date Stamp And Return To Our Courier

SKGF_DC1:185994.1

Nancy Feldman - Friday's Filings

From: Jay Sommerkamp
To: Everyone
Date: 10/14/03 2:25PM
Subject: Friday's Filings

FILE COPY

On Friday, the PTO had a power failure which complicated the filing process. The PTO had closed the office and we could only put the filings into a drop area. All SKGF filings were delivered to the PTO and put through the drop on a timely basis, but we found out we will have no postcards to prove this fact.

Do you wish to refile any of these filings tonight?

There were 4 Stat Bars due today which we should probably refile so that we can obtain a post card (2 PCT's, one response and one maintenance fee).

If you wish to refile, please contact Vita so she can put the filing on tonight's PTO list.

Sterne Kessler Goldstein Fox
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*Admitted only in Maryland
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October 10, 2003

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Commissioner for Patents
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Art Unit 1639

Re: U.S. Utility Patent Application
Appl. No. 09/987,456; Filed: November 14, 2001
For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**
Inventor: Zauderer *et al.*
Our Ref: 1821.0070004/EKS/EJH/T-M

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Preliminary Amendment Under 37 C.F.R. § 1.115 and Reply to Restriction Requirement; and
2. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Elizabeth J. Haanes, Ph.D.
Attorney for Applicants
Registration No. 42,613

EJH/T-M/nef
Enclosures

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 6770
Zauderer *et al.*	Art Unit: 1639
Appl. No. 09/987,456	Examiner: Epperson, J.D.
Filed: November 14, 2001	Atty. Docket: 1821.0070004/EJH/T-M
For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**	

Preliminary Amendment Under 37 C.F.R. §1.115 and Reply To Restriction Requirement

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

In advance of prosecution, Applicants submit the following amendments and remarks. This Preliminary Amendment is provided in the following format:

(A) Each section begins on a separate sheet;

(B) Starting on a separate sheet, amendments to the specification by presenting replacement paragraphs marked up to show changes made;

(C) Starting on a separate sheet, a complete listing of all of the claims;

- in ascending order;
- with status identifiers; and
- with markings in the currently amended claims;

(D) Starting on a separate sheet, the Remarks.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying

this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

84. (New) A method of selecting polynucleotides which encode an antigen-specific human immunoglobulin molecule, or antigen-specific fragment thereof, comprising:

(a) introducing into a population of mammalian host cells capable of expressing said immunoglobulin molecule and permissive for vaccinia virus infectivity, a first library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of first immunoglobulin subunit polypeptides, each first immunoglobulin subunit polypeptide comprising:

(i) a first immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light chain constant region or fragment thereof,

(ii) an immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said variable region corresponds to said first constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said first immunoglobulin subunit polypeptide,

wherein said first library is constructed in a vaccinia virus vector;

(b) introducing into said host cells a second library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of second immunoglobulin subunit polypeptides, each comprising:

(i) a second immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light chain constant region or fragment thereof, wherein said second immunoglobulin constant region is not the same as said first immunoglobulin constant region,

(ii) an immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said variable region corresponds to said second constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said second immunoglobulin subunit polypeptide,

wherein said second immunoglobulin subunit polypeptide is capable of combining with said first immunoglobulin subunit polypeptide to form an immunoglobulin molecule, or antigen-specific fragment thereof, and wherein said second library is constructed in a vaccinia virus vector;

(c) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(d) contacting said immunoglobulin molecules or fragments thereof with an antigen and detecting specific antigen-antibody complexes; and

(e) recovering vaccinia virus vectors containing polynucleotides of said first library which encode immunoglobulin subunit polypeptides which, as part of an

immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

85. (New) The method of claim 84, wherein the vaccinia virus vectors containing said second library of polynucleotides are rendered incapable of producing infectious vaccinia virus virions in said host cells.

86. (New) The method of claim 85, further comprising:

(f) introducing the vaccinia virus vectors recovered in (e) into a population of mammalian host cells capable of expressing said immunoglobulin molecule and permissive for vaccinia virus infectivity;

(g) introducing into said host cells said second library of polynucleotides;

(h) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(i) contacting said immunoglobulin molecules or fragments thereof with said antigen and detecting specific antigen-antibody complexes; and

(j) recovering vaccinia virus vectors containing polynucleotides of said first library which encode immunoglobulin subunit polypeptides which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

87. (New) The method of claim 86, further comprising repeating steps (f)-(j) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

88. (New) The method of claim 84, further comprising isolating the immunoglobulin subunit polypeptide-encoding polynucleotides contained in the vaccinia virus vectors recovered from said first library.

89. (New) The method of claim 88, further comprising:

(k) introducing into a population of mammalian host cells capable of expressing said immunoglobulin molecule and permissive for vaccinia virus infectivity vaccinia virus vectors containing said second library of polynucleotides, wherein said vaccinia virus vectors are infectious;

(l) introducing into said host cells vaccinia virus vectors containing those polynucleotides isolated from said first library, wherein the vaccinia virus vectors containing said isolated polynucleotides are rendered incapable of producing infectious vaccinia virus vectors in said host cells;

(m) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(n) contacting said immunoglobulin molecules or fragments thereof with said specific antigen and detecting specific antigen-antibody complexes; and

(o) recovering vaccinia virus vectors containing polynucleotides of said second library which encode immunoglobulin subunit polypeptides which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

90. (New) The method of claim 89, further comprising:

(p) introducing the vaccinia virus vectors recovered in (o) into a population of mammalian host cells capable of expressing said immunoglobulin molecule and permissive for vaccinia virus infectivity;

(q) introducing into said host cells vaccinia virus vectors containing those polynucleotides isolated from said first library, wherein the vaccinia virus vectors containing said isolated polynucleotides are rendered incapable of producing infectious vaccinia virus visions in said host cells;

(r) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(s) contacting said immunoglobulin molecules or fragments thereof with said antigen and detecting specific antigen-antibody complexes; and

(t) recovering vaccinia virus vectors containing polynucleotides of said second library which encode immunoglobulin subunit polypeptides which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

91. (New) The method of claim 90, further comprising repeating steps (p)-(t) one or more times, thereby enriching for polynucleotides of said second library which encode a second immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

92. (New) The method of claim 91, further comprising isolating the immunoglobulin subunit polypeptide-encoding polynucleotides contained in the vaccinia virus vectors recovered from said second library.

93. (New) A method of producing a first polynucleotide and a second polynucleotide which encode an antigen-specific human immunoglobulin molecule or an antigen-specific fragment thereof comprising combining a first polynucleotide and a second polynucleotide isolated according to claim 92.

94. (New) A method of producing a host cell which expresses an antigen-specific human immunoglobulin molecule or an antigen-specific fragment thereof comprising introducing the first and second polynucleotides produced as recited in claim 93 into a mammalian host cell capable of expressing said first and second polynucleotides.

95. (New) A method of producing an antigen-specific human immunoglobulin molecule or antigen-specific fragment thereof, comprising:

culturing a host cell produced according to the method of claim 94 under conditions wherein said first and second polynucleotides are expressed; and

recovering said antigen-specific human immunoglobulin molecule or antigen-specific fragment thereof.

96. (New) The method of claim 84, wherein said plurality of first immunoglobulin subunit polypeptides are immunoglobulin heavy chains, or fragments thereof.

97. (New) The method of claim 84, wherein said plurality of first immunoglobulin subunit polypeptides are immunoglobulin light chains, or fragments thereof.

98. (New) The method of claim 85, wherein said host cells are infected with said first library at an MOI ranging from about 1 to about 10, and wherein said second library is introduced under conditions which allow up to 20 vaccinia virus vectors of said second library to be taken up by each infected host cell.

99. (New) The method of claim 89, wherein said host cells are infected with said second library at an MOI ranging from about 1 to about 10.

100. (New) The method of claim 84, wherein said transcriptional control region comprises a poxvirus promoter.

101. (New) The method of claim 100, wherein said promoter is a vaccinia virus p7.5 promoter.

102. (New) The method of claim 100, wherein said promoter is a vaccinia MH-5 promoter.

103. (New) The method of claim 84, wherein said transcriptional control region comprises a T7 phage promoter active in cells in which T7 RNA polymerase is expressed.

104. (New) The method of claim 84, wherein said transcriptional control region comprises a transcriptional termination region.

105. (New)The method of claim 84, wherein said vaccinia virus vector is attenuated.

106. (New) The method of claim 105, wherein said vaccinia virus vector is deficient in D4R synthesis.

107. (New) The method of claim 84, wherein said first library of polynucleotides is constructed by a method comprising:

(a) cleaving an isolated vaccinia virus genome to produce a first viral fragment and a second viral fragment, wherein said first fragment is nonhomologous with said second fragment;

(b) providing a population of transfer plasmids comprising said polynucleotides which encode said plurality of immunoglobulin heavy or light chains, or fragments thereof through operable association with a transcription control region, flanked by a 5' flanking region and a 3' flanking region, wherein said 5' flanking region is homologous to a terminal portion of said first viral fragment and said 3' flanking region is homologous to a terminal portion of said second viral fragment; and wherein said transfer plasmids are capable of homologous recombination with said first and second viral fragments such that a viable vaccinia virus genome is formed;

(c) introducing said transfer plasmids and said first and second viral fragments into a mammalian host cell permissive for vaccinia virus infectivity under conditions wherein said transfer plasmids and said viral fragments undergo *in vivo* homologous recombination, thereby producing a viable modified vaccinia virus genome comprising a polynucleotide which encodes an immunoglobulin heavy chain, or fragment thereof, or an immunoglobulin light chain, or fragment thereof; and

(d) recovering said modified vaccinia virus genome.

108. (New) The method of claim 107, wherein said vaccinia virus genome is selected from the group consisting of a v7.5/tk virus genome and a vEL/tk virus genome

109. (New) The method of claim 107, wherein said first viral fragment and said second viral fragment are generated by cleaving unique NotI or ApaI restriction sites in the tk gene of said vaccinia virus genome.

110. (New) The method of claim 84, wherein said second library of polynucleotides is constructed by a method comprising:

(a) cleaving an isolated vaccinia virus genome to produce a first viral fragment and a second viral fragment, wherein said first fragment is nonhomologous with said second fragment;

(b) providing a population of transfer plasmids comprising said polynucleotides which encode said plurality of immunoglobulin light or heavy chains, or fragments thereof through operable association with a transcription control region, flanked by a 5' flanking region and a 3' flanking region, wherein said 5' flanking region is homologous to a terminal portion of said first viral fragment and said 3' flanking region is homologous to a terminal portion of said second viral fragment; and wherein said transfer plasmids are capable of homologous recombination with said first and second viral fragments such that a viable vaccinia virus genome is formed;

(c) introducing said transfer plasmids and said first and second viral fragments into a mammalian host cell permissive for vaccinia virus infectivity under conditions wherein said transfer plasmids and said viral fragments undergo homologous recombination, thereby producing a viable modified vaccinia virus genome comprising a polynucleotide which encodes an immunoglobulin light chain or fragment thereof or an immunoglobulin heavy chain, or fragment thereof; and

(d) recovering said modified vaccinia virus genome.

111. (New) The method of claim 110, wherein said vaccinia virus genome is selected from the group consisting of a v7.5/tk virus genome and a vEL/tk virus genome

112. (New) The method of claim 110, wherein said first viral fragment and said second viral fragment are generated by cleaving unique NotI or ApaI restriction sites in the tk gene of said vaccinia virus genome.

113. (New) The method of claim 96, wherein said immunoglobulin heavy chains, or fragments thereof are a secreted form of an immunoglobulin heavy chain, or fragment thereof.

114. (New) The method of claim 113,

wherein vaccinia virus vectors containing said first library of polynucleotides are divided into a plurality of virus pools, and each virus pool is infected into a separate population of mammalian host cells to form a plurality of host cell pools;

wherein said host cell pools are cultured such that immunoglobulin molecules, or antigen-specific fragments thereof, are expressed and secreted into the culture medium containing said host cell pools to form a plurality of immunoglobulin pools;

wherein said immunoglobulin pools are contacted with said antigen, and specific antigen-antibody complexes are detected; and

wherein vaccinia virus vectors are recovered from those host cell pools which expressed immunoglobulin pools from which specific antigen-antibody complexes were detected.

115. (New) The method of claim 114, further comprising:

(a) dividing said recovered vaccinia virus vectors into a plurality of virus sub-pools and infecting each virus sub-pool into a separate population of mammalian host cells to form a plurality of host cell sub-pools;

(b) culturing said host cell sub-pools such that immunoglobulin molecules, or antigen-specific fragments thereof are expressed and secreted into the culture medium containing said host cell sub-pools to form a plurality of immunoglobulin sub-pools;

(c) contacting said immunoglobulin sub-pools with said antigen, and detecting specific antigen-antibody complexes; and

(d) recovering vaccinia virus vectors from those host cell sub-pools which expressed immunoglobulin sub-pools from which specific antigen antibody complexes were detected.

116. (New) The method of claim 115, further comprising repeating steps (a)-(d) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

117. (New) The method of claim 97, wherein said second immunoglobulin subunit polypeptides are a secreted form of an immunoglobulin heavy chain, or fragment thereof.

118. (New) The method of claim 117,

wherein vaccinia virus vectors containing said first library of polynucleotides are divided into a plurality of virus pools, and each virus pool is infected into a separate population of mammalian host cells to form a plurality of host cell pools;

wherein said host cell pools are cultured such that immunoglobulin molecules, or antigen-specific fragments thereof are expressed and secreted into the culture medium containing said host cell pools to form a plurality of immunoglobulin pools;

wherein said immunoglobulin pools are contacted with said antigen, and specific antigen-antibody complexes are detected; and

wherein vaccinia virus vectors are recovered from those host cell pools which expressed immunoglobulin pools from which specific antigen antibody complexes were detected.

119. (New) The method of claim 118, further comprising:

(a) dividing said recovered vaccinia virus vectors into a plurality of virus sub-pools and infecting each virus sub-pool into a separate population of mammalian host cells to form a plurality of host cell sub-pools;

(b) culturing said host cell sub-pools such that immunoglobulin molecules, or antigen-specific fragments thereof are expressed and secreted into the culture medium containing said host cell sub-pools to form a plurality of immunoglobulin sub-pools;

(c) contacting said immunoglobulin sub-pools with said antigen, and detecting specific antigen-antibody complexes; and

(d) recovering vaccinia virus vectors from those host cell sub-pools which expressed immunoglobulin sub-pools from which specific antigen antibody complexes were detected.

120. (New) The method of claim 119, further comprising repeating steps (a)-(d) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

121. (New) The method of claim 114, wherein said detecting is by ELISA.

122. (New) The method of claim 118, wherein said detecting is by ELISA.

123. (New) An antibody, or antigen-specific fragment thereof, produced by the method of claim 84.

124. (New) A composition comprising the antibody of claim 123, and a pharmaceutically acceptable carrier.

125. (New) A host cell produced according to the method of claim 94.

126. (New) A kit for the selection of antigen-specific recombinant human immunoglobulins, or antigen-specific fragment thereof, expressed in a mammalian host cell permissive for vaccinia virus infectivity comprising:

(a) a first library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of first immunoglobulin subunit polypeptides, each first immunoglobulin subunit polypeptide comprising:

(i) a first immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light chain constant region or fragment thereof,

(ii) an immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said variable region corresponds to said first constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said first immunoglobulin subunit polypeptide,

wherein said first library is constructed in a vaccinia virus vector;

(b) a second library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of second immunoglobulin subunit polypeptides, each comprising:

(i) a second immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light

chain constant region or fragment thereof, wherein said second immunoglobulin constant region is not the same as said first immunoglobulin constant region,

(ii) an immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said variable region corresponds to said second constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said second immunoglobulin subunit polypeptide,

wherein said second immunoglobulin subunit polypeptide is capable of combining with said first immunoglobulin subunit polypeptide to form a surface immunoglobulin molecule, or antigen-specific fragment thereof, and wherein said second library is constructed in a vaccinia virus vector; and

(c) a population of mammalian host cells, wherein said cells are permissive for vaccinia virus infectivity and are capable of expressing said immunoglobulin molecules;

wherein at least one of said first and second libraries are provided as infectious vaccinia virus particles and either of said first or second libraries is optionally provided as inactivated vaccinia virus particles, and wherein said infectious and said inactivated virus particles infect said host cells and allow expression of said first and second immunoglobulin subunit polypeptides; and

wherein antigen-specific immunoglobulin molecules expressed by said host cells are selected through interaction with an antigen.

127. (New) A method of producing a library of polynucleotides which encode a plurality of human immunoglobulin subunit polypeptides in a vaccinia virus vector comprising:

(a) cleaving an isolated vaccinia virus genome to produce a first viral fragment and a second viral fragment, wherein said first fragment is nonhomologous with said second fragment;

(b) providing a population of transfer plasmids comprising a plurality of polynucleotides encoding, through operable association with a transcription control region, a plurality of immunoglobulin subunit polypeptides, flanked by a 5' flanking region and a 3' flanking region, wherein said 5' flanking region is homologous to said first viral fragment and said 3' flanking region is homologous to said second viral fragment; and wherein said transfer plasmids are capable of homologous recombination with said first and second viral fragments such that a viable virus genome is formed;

(c) introducing said transfer plasmids and said first and second viral fragments into a mammalian host cell under conditions wherein said transfer plasmids and said viral fragments undergo *in vivo* homologous recombination, thereby producing a plurality of viable modified virus genomes, each comprising a polynucleotide which encodes an immunoglobulin subunit polypeptide; and

(d) recovering said plurality of modified virus genomes.

128. (New) The method of claim 127 wherein each human immunoglobulin subunit polypeptide comprises:

(a) a first immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light chain constant region or fragment thereof;

(b) an immunoglobulin variable region corresponding to said first constant region; and

(c) a signal peptide capable of directing cell surface expression or secretion of said first immunoglobulin subunit polypeptide.

129. (New) The method of claim 84, wherein step (e) further comprises recovering vaccinia virus vectors containing polynucleotides of said second library which encode immunoglobulin subunit polypeptides which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

130. (New) The method of claim 129, further comprising isolating the immunoglobulin subunit polypeptide-encoding polynucleotides contained in the vaccinia virus vectors recovered from said second library.

131. (New) A method of producing a first polynucleotide and a second polynucleotide which encode an antigen-specific human immunoglobulin molecule or an antigen-specific fragment thereof comprising combining a first polynucleotide and a second polynucleotide isolated according to claim 130.

Remarks

Upon entry of the foregoing amendment, claims 84-131 are pending in the application, with claims 84, 126, and 127 being the independent claims. Claims 1-83 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 84-131 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Support for new claims 84-131 is found throughout the specification and claims as originally filed.

Reply to Restriction Requirement

In reply to the Office Action dated **September 10, 2003** (PTO Prosecution File Wrapper Paper No. 9), requesting an election of one group of claims to prosecute in the above-referenced patent application, Applicants hereby provisionally elect to prosecute the claims of Group I. It is believed that new claims 84-106, 113-122, and 129-131 fall within this group. This election is made without prejudice to or disclaimer of the other claims or inventions disclosed. Applicants reserve the right to pursue the nonelected claims in one or more divisional applications.

This election is made **with** traverse.

With respect to the Examiner's division of the claims into five groups and the reasons stated therefor, Applicants respectfully traverse. Each of the groups is related. For example, Groups I, II, and III are related as between a method of selecting from libraries of polynucleotides which encode an antigen-specific immunoglobulin molecule

(Group I), a method of constructing a library of polynucleotides which encode immunoglobulin subunit polypeptides (Group II), and a kit for selecting antigen-specific immunoglobulins from libraries of polynucleotides (Group III). Groups I-III are related to Group IV as between a method, and an immunoglobulin produced by that method. Likewise, Groups IV and V are related as between an antibody produced by a method of selecting polynucleotides which encode an antigen-specific immuoglobulin (Group IV) and a composition comprising an antibody produced by a method of selecting polynucleotides which encode an antigen-specific immuoglobulin and a pharmaceutically acceptable carrier (Group V).

Even assuming, *arguendo*, that Groups I-V represent distinct or independent inventions, Applicants submit that to search and examine the subject matter of these Groups together would not be a serious burden on the Examiner. In particular, any art related to a method of selecting from libaries of polynucleotides polynucleotides which encode an antigen-specific immunoglobulin molecule is very likely to overlap substantially with art related to a method of constructing a library of polynucleotides which encode immunoglobulin subunit polypeptides, and a kit for selecting antigen-specific immunoglobulins from libraries of polynucleotides. Similarly, art related to an antibody produced by a method of selecting polynucleotides which encode an antigen-specific immunoglobulin is very likely to substantially overlap with art related to a composition comprising an antibody produced by a method of selecting polynucleotides which encode an antigen-specific immuoglobulin and a pharmaceutically acceptable carrier. Accordingly, it would not be an undue burden for the Examiner to search, at a

minimum, Groups I, II, and II together, and Groups IV and V together. The M.P.E.P. §803 (Eighth Edition, Rev. August, 2001) states:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

Thus, in view of the M.P.E.P. §803, Applicants respectfully request that all claims be searched and examined in the subject application. Applicants retain the right to petition from the restriction requirement under 37 C.F.R. § 1.144.

Reconsideration and withdrawal of the Restriction Requirement, and consideration and allowance of all pending claims, are respectfully requested.

The Examiner has also required a large number of species elections. Applicants' provisional elections are listed below, along with a listing of each of the new claims believed to read on each of the provisionally-elected species.

These elections are made **with** traverse.

Subgroup 1. The Examiner has required an election of species among host cells. Applicants hereby provisionally elect to prosecute the species comprising a HeLa cell ~~which is permissive for the production of infectious viral particles. New claims 84-131~~ are generic to the provisionally elected species.

Subgroup 2. The Examiner has required an election of species among immunoglobulin sources. Applicants hereby elect to prosecute the species comprising a human immunoglobulin. New claims 84-131 specifically recite the elected species.

Subgroup 3. The Examiner has required an election of species among immunoglobulins. Applicants hereby provisionally elect to prosecute the species comprising a secreted form of immunoglobulin. New claims 84-112 and 123-131 are

elected species. New claims 121 and 122 specifically recite the provisionally elected species.

Subgroup 8. The Examiner has required an election of species among antigen attachment. Applicants hereby provisionally elect to prosecute the species comprising attachment to a solid surface, such as a well of an ELISA plate. New claims 84-120 and 123-131 are generic to the provisionally elected species. New claims 121 and 122 specifically recite the provisionally elected species.

Applicants respectfully traverse and request the withdrawal of the requirement for election of species. As a threshold matter, Applicants point out that MPEP § 803 lists the criteria for a proper restriction requirement:

> Under the statute an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP § 806.04 – § 806.04(i)) or distinct (MPEP § 806.05 – § 806.05(i)).
>
> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

Thus, even assuming, *arguendo*, that the groups listed by the Examiner represent patentably distinct species, restriction remains improper unless it can be shown that the search and examination of the listed groups would entail a "serious burden." *See* M.P.E.P. § 803. In the present situation, no such showing has been made. For example, although the Examiner has asserted that embodiments referring to immunoglobulins are distinct species, Applicants submit that a search of IgG as an immunoglobulin would provide useful information regarding other types of immunoglobulin, such as IgM.

Similarly, the search and examination of all of the claims of Group I would not entail a serious burden.

Applicants assert the right to claim additional embodiments in the event that a generic claim thereto is found to be allowable in accordance with 37 C.F.R. § 1.141(a). Reconsideration and withdrawal of the Requirement for Election of species, and consideration and allowance of all pending claims, are respectfully requested.

Summary

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Elizabeth J. Haanes, Ph.D.
Attorney for Applicants
Registration No. 42,613

Date: 10 October, 2003

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

* * * COMMUNICATION RESULT REPORT (OCT. 31. 2003 3:02PM) * * *

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ILE MODE	OPTION	ADDRESS (GROUP)	RESULT	PAGE
706 MEMORY TX		3968#18210070004#7033084407#	OK	3/3

REASON FOR ERROR
E-1) HANG UP OR LINE FAIL
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E-3) NO ANSWER
E-4) NO FACSIMILE CONNECTION

Re-fax of pages 2+12 of Reply follow.

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Sterne Kessler Goldstein Fox
ATTORNEYS AT LAW

Fax

☒Urgent ☒ Return reply requested ☐ Original will be sent as confirmation

To: Patent Technology Center 1600

Date: October 31, 2003

Attention: Renee

Re: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

From: Elizabeth J. Haanes, Ph.D.

Pages (including cover sheet): **30**

Your Reference:

Fax No: 703-308-4407

Our Reference: 1821.0070004/EJH/T-M

* * * COMMUNICATION RESULT REPORT (OCT. 31. 2003 3:07PM) * * *

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ILE MODE	OPTION	ADDRESS (GROUP)	RESULT	PAGE
707 MEMORY TX		3968#18210070004#7033084407#	OK	3/3

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To: Patent Technology Center 1600

Date: October 31, 2003

Attention: Renee

Re: *In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells

From: Elizabeth J. Haanes, Ph.D. ejh

Pages (including cover sheet): ~~30~~ 3

Your Reference:

Fax No: 703-308-4407

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Message

Per your telephone conversation with Tracy Muller of our office, attached is a copy of the Preliminary Amendment and Reply to Restriction Requirement as filed in person at the U. S. Patent & Trademark Office on Friday, October 10, 2003, along with a copy of the page of the daily filing log book from that date indicating that the filing was delivered.

please sign and return this page as acknowledgment of receipt

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		Due Da	October 10, 2003
Applicants:	.der.. *et al.*	**A Unit:**	1639
		Examiner:	Epperson, J.D.
Application No.:	09/987,456	**Docket:**	1821.0070004
Filed:	November 14, 2001	**Atty:**	EJH/T-M

For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. SKGF Cover Letter;
2. Preliminary Amendment Under 37 C.F.R. § 1.115 and Reply to Restriction Requirement; and
3. One (1) return postcard.

Please Date Stamp And Return To Our Courier

SKGF_DC1:185994.1

From: Jay Sommerkamp
To: Everyone
Date: 10/14/03 2:25PM
Subject: Friday's Filings

FILE COPY

On Friday, the PTO had a power failure which complicated the filing process. The PTO had closed the office and we could only put the filings into a drop area. All SKGF filings were delivered to the PTO and put through the drop on a timely basis, but we found out we will have no postcards to prove this fact.

Do you wish to refile any of these filings tonight?

There were 4 Stat Bars due today which we should probably refile so that we can obtain a post card (2 PCT's, one response and one maintenance fee).

If you wish to refile, please contact Vita so she can put the filing on tonight's PTO list.

Oct 10 2003
1:30 PM

Gomez 1875.06/orm (Lmy) 10/040,376 Req Cont Exam
Pet For Ext, Copy of Amendment & Reply, FILS T
Supplemental C/C payment Form

CM 1735.04/0001 (RLS) 09/709,420 Amendment & Reply

** Zauderer 1821.0070004 (TM) 09/187,456 Prelim Amendment
& Reply to Restr Reqmt

Fikes 2060.005/006 (PAC) 10/149,137 Reply to Notice
of Defective Resp., Amend & Substitute Sea
Listing, Disk & Paper Copy of Sea Listing

Brasch 0942.50/0001 (VKM) 09/695,405 Reply to Reasons
for Exam, Pet For Ext, Form 6 Suppl IDS &
C/C payment Form

Cornerstone 1834.028/C03 (MLP) PCT/US03/27331 Submission
of Payment of Transmittal Fee, Sch Fee, Intl Fee
& Priority Doc Fee & C/C payment Form

Kung 1684.049/C02 (RLS) PCT/US03/07935 CIPT II Demand
& C/C payment Form

Jack Lab 1710.455/0000 (TJS) TBA New TM Applin
& C/C payment Form

* * * COMMUNICATION RESULT REPORT (OCT. 31. 2003 3:25PM) * * *

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708 MEMORY TX		3968#18210070004#7033084407#	OK	2/2

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********** -COMM JURNAL- ********** DATE DEC-11-200 *** TIME 15:24 ********

MODE = MEMORY TRANSMISSION START=DEC-11 14:58 END=DEC-11 15:24

FILE NO.=833

STN NO.	COMM.	ONE-TOUCH/ ABBR NO.	STATION NAME/TEL NO.	PAGES	DURATION
001	OK	a	3968#18210070004#7037469214#	032/032	00:10:25
002	OK	a	3968#18210070004#703[illegible]87922#	032/032	00:13:57

********** -S K G F - ***** - 202 371 2540- **********

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Sterne Kessler Goldstein Fox
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Fax ☒Urgent ☐ Return reply requested ☐ Original will be sent as confirmation

To: U.S. Patent and Trademark Office

Date: December 11, 2003

Attention: **Examiner J.D. Epperson**

Re: U.S. Appl. No. 09/987,456;
Filed: Nov. 14, 2001

For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

From: Elizabeth J. Haanes, Ph.D. ejh
Reg # 42,613

Pages (including cover sheet): 32

Your Reference:

Fax Nos: 703-746-9214 and 703-308-7922

Our Reference: 1821.0070004/EJH/T-M

Message

Per your telephone conversation with Tracy Muller of our office, attached is a copy of the Preliminary Amendment and Reply to Restriction Requirement as filed in person at the U. S. Patent & Trademark Office on Friday, October 10, 2003, a copy of the page of the daily filing log book from that date indicating that the filing was delivered, and our previous fax cover sheet and transmission report confirming submission of those documents to Renee on October 31, 2003.

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Sterne Kessler Goldstein Fox
ATTORNEYS AT LAW

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To: U.S. Patent and Trademark Office

Date: December 11, 2003

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Re: U.S. Appl. No. 09/987,456;
Filed: Nov. 14, 2001
For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

From: Elizabeth J. Haanes, Ph.D. Reg # 42,663

Pages (including cover sheet): **32**

Your Reference:

Fax Nos: 703-746-9214 and 703-308-7922

Our Reference: 1821.0070004/EJH/T-M

Message

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United States Patent and Trademark Office

PATENT APPLICATION INFORMATION RETRIEVAL

Search results for application number:09/987,456			
Application Number:	09/987,456	Customer Number:	-
Filing or 371(c) Date:	11-14-2001	Status:	Response to Non-Final Office Action Entered and Forwarded to Examiner
Application Type:	Utility	Status Date:	12-19-2003
Examiner Name:	EPPERSON, JON D	Location:	ELECTRONIC
Group Art Unit:	1639	Location Date:	12-23-2003
Confirmation Number:	6770	Earliest Publication No:	US 2002-0123057 A1
Attorney Docket Number:	1821.0070004/EKS/EJH/TAC	Earliest Publication Date:	09-05-2002
Class/ Sub-Class:	435/007.1	Patent Number:	-
First Named Inventor:	Maurice Zauderer, Pittsford, NY (US)	Issue Date of Patent:	-
Title Of Invention:	In vitro methods of producing and identifying immunoglobulin molecules in eukaryotic cells		

Continuity Data | Published Documents

File Contents History

Number	Date	Contents Description
23	12-19-2003	IFW Amended case processing Complete
22	12-19-2003	Date Forwarded to Examiner
21	10-10-2003	Response to Election / Restriction Filed
20	09-10-2003	Mail Restriction Requirement
19	09-08-2003	Requirement for Restriction / Election
18	05-01-2003	Information Disclosure Statement (IDS) Filed
17	05-28-2002	Information Disclosure Statement (IDS) Filed
16	11-06-2002	Information Disclosure Statement (IDS) Filed
15	10-04-2002	Case Docketed to Examiner in GAU
14	07-12-2002	Case Docketed to Examiner in GAU
13	06-12-2002	Preliminary Amendment
12	06-05-2002	Case Docketed to Examiner in GAU
11	04-27-2002	Case Docketed to Examiner in GAU
10	03-22-2002	Application Dispatched from OIPE
9	03-22-2002	Application Is Now Complete
7	02-21-2002	A payment by the applicant to cover the cost of basic filing, claims, is fees, etc.

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Paper No.

Notice of Non-Compliant Amendment (37 CFR 1.121)

The amendment document filed on 12/11/03 is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). In order for the amendment document to be compliant, correction of the following item(s) is required. **Only the corrected section of the non-compliant amendment document must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment document must be re-submitted.** 37 CFR 1.121(h).

THE FOLLOWING CHECKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

☐ 1. Amendments to the specification:
- ☐ A. Amended paragraph(s) do not include markings.
- ☐ B. New paragraph(s) should not be underlined.
- ☐ C. Other _____

☐ 2. Abstract:
- ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
- ☐ B. Other _____

☐ 3. Amendments to the drawings: _____

☒ 4. Amendments to the claims:
- ☒ A. A complete listing of all of the claims is not present.
- ☐ B. The listing of claims does not include the text of all claims (including withdrawn claims)
- ☐ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified.
- ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
- ☐ E. Other: _____

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP Sec. 714 and the USPTO website at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officeflyer.pdf

If the non-compliant amendment is a **PRELIMINARY AMENDMENT,** applicant is given ONE MONTH from the mail date of this letter to supply the corrected section which complies with 37 CFR 1.121. Failure to comply with 37 CFR 1.121 will result in non-entry of the preliminary amendment and examination on the merits will commence without consideration of the proposed changes in the preliminary amendment(s). This notice is not an action under 35 U.S.C. 132, and **this ONE MONTH time limit is not extendable.**

If the non-compliant amendment is a reply to a **NON-FINAL OFFICE ACTION (including a submission for an RCE),** and since the amendment appears to be a *bona fide* attempt to be a reply (37 CFR 1.135(c)), applicant is given a TIME PERIOD of ONE MONTH from the mailing of this notice within which to re-submit the corrected section which complies with 37 CFR 1.121 in order to avoid abandonment. **EXTENSIONS OF THIS TIME PERIOD ARE AVAILABLE UNDER 37 CFR 1.136(a).**

If the amendment is a reply to a **FINAL REJECTION,** this form may be an attachment to an Advisory Action. **The period for response to a final rejection continues to run from the date set in the final rejection**, and is not affected by the non-compliant status of the amendment.

Maria G. Hammond — Legal Instruments Examiner (LIE)

571-272-0561 — Telephone No.

United States Patent and Trademark Office

PATENT APPLICATION INFORMATION RETRIEVAL

Search results for application number:09/987,456

Application Number:	09/987,456	Customer Number:	-
Filing or 371(c) Date:	11-14-2001	Status:	Non Final A Mailed
Application Type:	Utility	Status Date:	02-11-2004
Examiner Name:	EPPERSON, JON D	Location:	ELECTRON
Group Art Unit:	1639	Location Date:	12-30-2003
Confirmation Number:	6770	Earliest Publication No:	US 2002-01 A1
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Class/ Sub-Class:	435/007.1	Patent Number:	-
First Named Inventor:	Maurice Zauderer, Pittsford, NY (US)	Issue Date of Patent:	-
Title Of Invention:	In vitro methods of producing and identifying immunoglobulin molecules in eukaryotic cells		

Select Search Option

Continuity Data
Published Documents

Search

File History

Number	Date	Contents Description
26	02-11-2004	Mail Notice of Informal or Non-Responsive Amendment
25	02-11-2004	Date Forwarded to Examiner
24	12-11-2003	Supplemental Response
23	12-19-2003	IFW Amended case processing Complete
22	12-19-2003	Date Forwarded to Examiner
21.1	10-10-2003	Informal or Non-Responsive Amendment after Examiner Actio
21	10-10-2003	Response to Election / Restriction Filed
20	09-10-2003	Mail Restriction Requirement
19	09-08-2003	Requirement for Restriction / Election
18	05-01-2003	Information Disclosure Statement (IDS) Filed
17	05-28-2002	Information Disclosure Statement (IDS) Filed
16	11-06-2002	Information Disclosure Statement (IDS) Filed
15	10-04-2002	Case Docketed to Examiner in GAU
14	07-12-2002	Case Docketed to Examiner in GAU
13	06-12-2002	Preliminary Amendment
12	06-05-2002	Case Docketed to Examiner in GAU
11	04-27-2002	Case Docketed to Examiner in GAU
10	03-22-2002	Application Dispatched from OIPE

Applicants: Zauderer *et al.*

Application No.: 09/987,456

Filed: November 14, 2001

For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

Due Date: March 11, 2004
Art Unit: 1639
Examiner: Epperson, J.D.
Docket: 1821.0070004
Atty: EKS/EJH/T-M

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. SKGF Cover Letter;
2. Supplemental Reply Under 37 C.F.R. § 1.121; and
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230449.1

Applicants: Zauderer *et al.*

Application No.: 09/987,456

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February 13, 2004

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Art Unit 1639

Re: U.S. Utility Patent Application
Appl. No. 09/987,456; Filed: November 14, 2001
For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**
Inventors: Zauderer *et al.*
Our Ref: 1821.0070004/EKS/EJH/T-M

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Supplemental Reply Under 37 C.F.R. § 1.121; and
2. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

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EJH/lam
Enclosures

230445.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 6770
Zauderer *et al.*	Art Unit: 1639
Appl. No. 09/987,456	Examiner: Epperson, J.D.
Filed: November 14, 2001	Atty. Docket: 1821.0070004/EJH/T-M
For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**	

Supplemental Reply under 37 C.F.R. § 1.121

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Mail Stop Non-Fee Amendment

Sir:

In reply to the Notice of Non-Compliant Amendment dated February 11, 2004 (hereinafter "the Notice"), and supplemental to Applicants' Amendment and Reply filed in this matter on October 10, 2003,[1] Applicants submit the following remarks. In accordance with 37 C.F.R. § 1.121(h), and as stated on the Notice, only the corrected section of the non-compliant amendment is being resubmitted in its entirety. Specifically, since the Notice indicated that the Amendments to the Claims section was non-compliant only because a complete listing of all the claims was not present, this Supplemental Reply provides a complete listing of all the claims. Applicants'

[1]The Notice refers to the Amendment and Reply filed on December 11, 2003. The Amendment and Reply was originally filed on October 10, 2003, and was resubmitted on December 11, 2003, because the originally-filed Amendment and Reply was misplaced by the USPTO. The USPTO requested resubmission multiple times following Applicants' diligent inquiries when the filing did not appear on the PAIR system. The first resubmission was sent via facsimile to the 1600 Tech Center on October 31, 2003. The second resubmission was sent via facsimile to the Examiner's attention on December 11, 2003.

Amendment and Reply filed on October 10, 2003, is otherwise reiterated and incorporated by reference herein.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1-83. (Cancelled)

84. (New) A method of selecting polynucleotides which encode an antigen-specific human immunoglobulin molecule, or antigen-specific fragment thereof, comprising:

(a) introducing into a population of mammalian host cells capable of expressing said immunoglobulin molecule and permissive for vaccinia virus infectivity, a first library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of first immunoglobulin subunit polypeptides, each first immunoglobulin subunit polypeptide comprising:

(i) a first immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light chain constant region or fragment thereof,

(ii) an immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said variable region corresponds to said first constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said first immunoglobulin subunit polypeptide,

wherein said first library is constructed in a vaccinia virus vector;

(b) introducing into said host cells a second library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of second immunoglobulin subunit polypeptides, each comprising:

(i) a second immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light chain constant region or fragment thereof, wherein said second immunoglobulin constant region is not the same as said first immunoglobulin constant region,

(ii) an immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said variable region corresponds to said second constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said second immunoglobulin subunit polypeptide,

wherein said second immunoglobulin subunit polypeptide is capable of combining with said first immunoglobulin subunit polypeptide to form an immunoglobulin molecule, or antigen-specific fragment thereof, and wherein said second library is constructed in a vaccinia virus vector;

(c) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(d) contacting said immunoglobulin molecules or fragments thereof with an antigen and detecting specific antigen-antibody complexes; and

(e) recovering vaccinia virus vectors containing polynucleotides of said first library which encode immunoglobulin subunit polypeptides which, as part of an

immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

85. (New) The method of claim 84, wherein the vaccinia virus vectors containing said second library of polynucleotides are rendered incapable of producing infectious vaccinia virus virions in said host cells.

86. (New) The method of claim 85, further comprising:

(f) introducing the vaccinia virus vectors recovered in (e) into a population of mammalian host cells capable of expressing said immunoglobulin molecule and permissive for vaccinia virus infectivity;

(g) introducing into said host cells said second library of polynucleotides;

(h) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(i) contacting said immunoglobulin molecules or fragments thereof with said antigen and detecting specific antigen-antibody complexes; and

(j) recovering vaccinia virus vectors containing polynucleotides of said first library which encode immunoglobulin subunit polypeptides which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

87. (New) The method of claim 86, further comprising repeating steps (f)-(j) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

88. (New) The method of claim 84, further comprising isolating the immunoglobulin subunit polypeptide-encoding polynucleotides contained in the vaccinia virus vectors recovered from said first library.

89. (New) The method of claim 88, further comprising:

(k) introducing into a population of mammalian host cells capable of expressing said immunoglobulin molecule and permissive for vaccinia virus infectivity vaccinia virus vectors containing said second library of polynucleotides, wherein said vaccinia virus vectors are infectious;

(l) introducing into said host cells vaccinia virus vectors containing those polynucleotides isolated from said first library, wherein the vaccinia virus vectors containing said isolated polynucleotides are rendered incapable of producing infectious vaccinia virus vectors in said host cells;

(m) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(n) contacting said immunoglobulin molecules or fragments thereof with said specific antigen and detecting specific antigen-antibody complexes; and

(o) recovering vaccinia virus vectors containing polynucleotides of said second library which encode immunoglobulin subunit polypeptides which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

90. (New) The method of claim 89, further comprising:

(p) introducing the vaccinia virus vectors recovered in (o) into a population of mammalian host cells capable of expressing said immunoglobulin molecule and permissive for vaccinia virus infectivity;

(q) introducing into said host cells vaccinia virus vectors containing those polynucleotides isolated from said first library, wherein the vaccinia virus vectors containing said isolated polynucleotides are rendered incapable of producing infectious vaccinia virus visions in said host cells;

(r) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(s) contacting said immunoglobulin molecules or fragments thereof with said antigen and detecting specific antigen-antibody complexes; and

(t) recovering vaccinia virus vectors containing polynucleotides of said second library which encode immunoglobulin subunit polypeptides which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

91. (New) The method of claim 90, further comprising repeating steps (p)-(t) one or more times, thereby enriching for polynucleotides of said second library which encode a second immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

92. (New) The method of claim 91, further comprising isolating the immunoglobulin subunit polypeptide-encoding polynucleotides contained in the vaccinia virus vectors recovered from said second library.

93. (New) A method of producing a first polynucleotide and a second polynucleotide which encode an antigen-specific human immunoglobulin molecule or an antigen-specific fragment thereof comprising combining a first polynucleotide and a second polynucleotide isolated according to claim 92.

94. (New) A method of producing a host cell which expresses an antigen-specific human immunoglobulin molecule or an antigen-specific fragment thereof comprising introducing the first and second polynucleotides produced as recited in claim 93 into a mammalian host cell capable of expressing said first and second polynucleotides.

95. (New) A method of producing an antigen-specific human immunoglobulin molecule or antigen-specific fragment thereof, comprising:

culturing a host cell produced according to the method of claim 94 under conditions wherein said first and second polynucleotides are expressed; and

recovering said antigen-specific human immunoglobulin molecule or antigen-specific fragment thereof.

96. (New) The method of claim 84, wherein said plurality of first immunoglobulin subunit polypeptides are immunoglobulin heavy chains, or fragments thereof.

97. (New) The method of claim 84, wherein said plurality of first immunoglobulin subunit polypeptides are immunoglobulin light chains, or fragments thereof.

98. (New) The method of claim 85, wherein said host cells are infected with said first library at an MOI ranging from about 1 to about 10, and wherein said second library is introduced under conditions which allow up to 20 vaccinia virus vectors of said second library to be taken up by each infected host cell.

99. (New) The method of claim 89, wherein said host cells are infected with said second library at an MOI ranging from about 1 to about 10.

100. (New) The method of claim 84, wherein said transcriptional control region comprises a poxvirus promoter.

101. (New) The method of claim 100, wherein said promoter is a vaccinia virus p7.5 promoter.

102. (New) The method of claim 100, wherein said promoter is a vaccinia MH-5 promoter.

103. (New) The method of claim 84, wherein said transcriptional control region comprises a T7 phage promoter active in cells in which T7 RNA polymerase is expressed.

104. (New) The method of claim 84, wherein said transcriptional control region comprises a transcriptional termination region.

105. (New)The method of claim 84, wherein said vaccinia virus vector is attenuated.

106. (New) The method of claim 105, wherein said vaccinia virus vector is deficient in D4R synthesis.

107. (New) The method of claim 84, wherein said first library of polynucleotides is constructed by a method comprising:

(a) cleaving an isolated vaccinia virus genome to produce a first viral fragment and a second viral fragment, wherein said first fragment is nonhomologous with said second fragment;

(b) providing a population of transfer plasmids comprising said polynucleotides which encode said plurality of immunoglobulin heavy or light chains, or fragments thereof through operable association with a transcription control region, flanked by a 5' flanking region and a 3' flanking region, wherein said 5' flanking region is homologous to a terminal portion of said first viral fragment and said 3' flanking region is homologous to a terminal portion of said second viral fragment; and wherein said transfer plasmids are capable of homologous recombination with said first and second viral fragments such that a viable vaccinia virus genome is formed;

(c) introducing said transfer plasmids and said first and second viral fragments into a mammalian host cell permissive for vaccinia virus infectivity under conditions wherein said transfer plasmids and said viral fragments undergo *in vivo* homologous recombination, thereby producing a viable modified vaccinia virus genome comprising a polynucleotide which encodes an immunoglobulin heavy chain, or fragment thereof, or an immunoglobulin light chain, or fragment thereof; and

(d) recovering said modified vaccinia virus genome.

108. (New) The method of claim 107, wherein said vaccinia virus genome is selected from the group consisting of a v7.5/tk virus genome and a vEL/tk virus genome

109. (New) The method of claim 107, wherein said first viral fragment and said second viral fragment are generated by cleaving unique NotI or ApaI restriction sites in the tk gene of said vaccinia virus genome.

110. (New) The method of claim 84, wherein said second library of polynucleotides is constructed by a method comprising:

(a) cleaving an isolated vaccinia virus genome to produce a first viral fragment and a second viral fragment, wherein said first fragment is nonhomologous with said second fragment;

(b) providing a population of transfer plasmids comprising said polynucleotides which encode said plurality of immunoglobulin light or heavy chains, or fragments thereof through operable association with a transcription control region, flanked by a 5' flanking region and a 3' flanking region, wherein said 5' flanking region is homologous to a terminal portion of said first viral fragment and said 3' flanking region is homologous to a terminal portion of said second viral fragment; and wherein said transfer plasmids are capable of homologous recombination with said first and second viral fragments such that a viable vaccinia virus genome is formed;

(c) introducing said transfer plasmids and said first and second viral fragments into a mammalian host cell permissive for vaccinia virus infectivity under conditions wherein said transfer plasmids and said viral fragments undergo homologous recombination, thereby producing a viable modified vaccinia virus genome comprising a polynucleotide which encodes an immunoglobulin light chain or fragment thereof or an immunoglobulin heavy chain, or fragment thereof; and

(d) recovering said modified vaccinia virus genome.

111. (New) The method of claim 110, wherein said vaccinia virus genome is selected from the group consisting of a v7.5/tk virus genome and a vEL/tk virus genome

112. (New) The method of claim 110, wherein said first viral fragment and said second viral fragment are generated by cleaving unique NotI or ApaI restriction sites in the tk gene of said vaccinia virus genome.

113. (New) The method of claim 96, wherein said immunoglobulin heavy chains, or fragments thereof are a secreted form of an immunoglobulin heavy chain, or fragment thereof.

114. (New) The method of claim 113,

wherein vaccinia virus vectors containing said first library of polynucleotides are divided into a plurality of virus pools, and each virus pool is infected into a separate population of mammalian host cells to form a plurality of host cell pools;

wherein said host cell pools are cultured such that immunoglobulin molecules, or antigen-specific fragments thereof, are expressed and secreted into the culture medium containing said host cell pools to form a plurality of immunoglobulin pools;

wherein said immunoglobulin pools are contacted with said antigen, and specific antigen-antibody complexes are detected; and

wherein vaccinia virus vectors are recovered from those host cell pools which expressed immunoglobulin pools from which specific antigen-antibody complexes were detected.

115. (New) The method of claim 114, further comprising:

(a) dividing said recovered vaccinia virus vectors into a plurality of virus sub-pools and infecting each virus sub-pool into a separate population of mammalian host cells to form a plurality of host cell sub-pools;

(b) culturing said host cell sub-pools such that immunoglobulin molecules, or antigen-specific fragments thereof are expressed and secreted into the culture medium containing said host cell sub-pools to form a plurality of immunoglobulin sub-pools;

(c) contacting said immunoglobulin sub-pools with said antigen, and detecting specific antigen-antibody complexes; and

(d) recovering vaccinia virus vectors from those host cell sub-pools which expressed immunoglobulin sub-pools from which specific antigen antibody complexes were detected.

116. (New) The method of claim 115, further comprising repeating steps (a)-(d) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

117. (New) The method of claim 97, wherein said second immunoglobulin subunit polypeptides are a secreted form of an immunoglobulin heavy chain, or fragment thereof.

118. (New) The method of claim 117,

wherein vaccinia virus vectors containing said first library of polynucleotides are divided into a plurality of virus pools, and each virus pool is infected into a separate population of mammalian host cells to form a plurality of host cell pools;

wherein said host cell pools are cultured such that immunoglobulin molecules, or antigen-specific fragments thereof are expressed and secreted into the culture medium containing said host cell pools to form a plurality of immunoglobulin pools;

wherein said immunoglobulin pools are contacted with said antigen, and specific antigen-antibody complexes are detected; and

wherein vaccinia virus vectors are recovered from those host cell pools which expressed immunoglobulin pools from which specific antigen antibody complexes were detected.

119. (New) The method of claim 118, further comprising:

(a) dividing said recovered vaccinia virus vectors into a plurality of virus sub-pools and infecting each virus sub-pool into a separate population of mammalian host cells to form a plurality of host cell sub-pools;

(b) culturing said host cell sub-pools such that immunoglobulin molecules, or antigen-specific fragments thereof are expressed and secreted into the culture medium containing said host cell sub-pools to form a plurality of immunoglobulin sub-pools;

(c) contacting said immunoglobulin sub-pools with said antigen, and detecting specific antigen-antibody complexes; and

(d) recovering vaccinia virus vectors from those host cell sub-pools which expressed immunoglobulin sub-pools from which specific antigen antibody complexes were detected.

120. (New) The method of claim 119, further comprising repeating steps (a)-(d) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

121. (New) The method of claim 114, wherein said detecting is by ELISA.

122. (New) The method of claim 118, wherein said detecting is by ELISA.

123. (New) An antibody, or antigen-specific fragment thereof, produced by the method of claim 84.

124. (New) A composition comprising the antibody of claim 123, and a pharmaceutically acceptable carrier.

125. (New) A host cell produced according to the method of claim 94.

126. (New) A kit for the selection of antigen-specific recombinant human immunoglobulins, or antigen-specific fragment thereof, expressed in a mammalian host cell permissive for vaccinia virus infectivity comprising:

(a) a first library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of first immunoglobulin subunit polypeptides, each first immunoglobulin subunit polypeptide comprising:

(i) a first immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light chain constant region or fragment thereof,

(ii) an immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said variable region corresponds to said first constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said first immunoglobulin subunit polypeptide,

wherein said first library is constructed in a vaccinia virus vector;

(b) a second library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of second immunoglobulin subunit polypeptides, each comprising:

(i) a second immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light

chain constant region or fragment thereof, wherein said second immunoglobulin constant region is not the same as said first immunoglobulin constant region,

(ii) an immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said variable region corresponds to said second constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said second immunoglobulin subunit polypeptide,

wherein said second immunoglobulin subunit polypeptide is capable of combining with said first immunoglobulin subunit polypeptide to form a surface immunoglobulin molecule, or antigen-specific fragment thereof, and wherein said second library is constructed in a vaccinia virus vector; and

(c) a population of mammalian host cells, wherein said cells are permissive for vaccinia virus infectivity and are capable of expressing said immunoglobulin molecules;

wherein at least one of said first and second libraries are provided as infectious vaccinia virus particles and either of said first or second libraries is optionally provided as inactivated vaccinia virus particles, and wherein said infectious and said inactivated virus particles infect said host cells and allow expression of said first and second immunoglobulin subunit polypeptides; and

wherein antigen-specific immunoglobulin molecules expressed by said host cells are selected through interaction with an antigen.

127. (New) A method of producing a library of polynucleotides which encode a plurality of human immunoglobulin subunit polypeptides in a vaccinia virus vector comprising:

(a) cleaving an isolated vaccinia virus genome to produce a first viral fragment and a second viral fragment, wherein said first fragment is nonhomologous with said second fragment;

(b) providing a population of transfer plasmids comprising a plurality of polynucleotides encoding, through operable association with a transcription control region, a plurality of immunoglobulin subunit polypeptides, flanked by a 5' flanking region and a 3' flanking region, wherein said 5' flanking region is homologous to said first viral fragment and said 3' flanking region is homologous to said second viral fragment; and wherein said transfer plasmids are capable of homologous recombination with said first and second viral fragments such that a viable virus genome is formed;

(c) introducing said transfer plasmids and said first and second viral fragments into a mammalian host cell under conditions wherein said transfer plasmids and said viral fragments undergo *in vivo* homologous recombination, thereby producing a plurality of viable modified virus genomes, each comprising a polynucleotide which encodes an immunoglobulin subunit polypeptide; and

(d) recovering said plurality of modified virus genomes.

128. (New) The method of claim 127 wherein each human immunoglobulin subunit polypeptide comprises:

(a) a first immunoglobulin constant region selected from the group consisting of a heavy chain constant region or fragment thereof and a light chain constant region or fragment thereof;

(b) an immunoglobulin variable region corresponding to said first constant region; and

(c) a signal peptide capable of directing cell surface expression or secretion of said first immunoglobulin subunit polypeptide.

129. (New) The method of claim 84, wherein step (e) further comprises recovering vaccinia virus vectors containing polynucleotides of said second library which encode immunoglobulin subunit polypeptides which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, are specific for said antigen.

130. (New) The method of claim 129, further comprising isolating the immunoglobulin subunit polypeptide-encoding polynucleotides contained in the vaccinia virus vectors recovered from said second library.

131. (New) A method of producing a first polynucleotide and a second polynucleotide which encode an antigen-specific human immunoglobulin molecule or an antigen-specific fragment thereof comprising combining a first polynucleotide and a second polynucleotide isolated according to claim 130.

Remarks

Upon entry of the foregoing amendment, claims 84-131 are pending in the application, with claims 84, 126, and 127 being the independent claims. Claims 1-83 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 84-131 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Support for new claims 84-131 is found throughout the specification and claims as originally filed.

Summary

In the Notice of Non-Compliant Amendment dated February 11, 2004, Applicants' Amendment and Reply filed in this matter on October 10, 2003 (see footnote 1, *supra*), was held to be non-compliant only because a complete listing of all the claims was not present. As stated on the Notice, only the corrected section of the non-compliant amendment was required to be resubmitted in its entirety. *See* 37 C.F.R. § 1.121(*h*). Since the present Supplemental Amendment and Reply provides a complete listing of all the claims in the present application, Applicants respectfully submit that the present Reply is fully responsive to the Notice. Applicants' Amendment and Reply filed on October 10, 2003, including all of the attachments thereto, is otherwise reiterated and incorporated by reference herein.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional

extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. 19-0036.

Respectfully submitted,

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Date: February 13, 2004

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